fragments are understood in particular as those amino acid sequences which correspond to at least 70 % of the sequence YPYDVPDYA or are shortened by at least one to two terminal amino acids.

In order to produce the monoclonal antibodies, small mammals, preferably rats, such as e.g. Lou/C rats or mice such as e.g. BalbC mice or rabbits are immunized with a HA peptide synthesized by standard methods. An uncoupled HA peptide or a HA peptide which is optionally coupled N-terminally or C-terminally to a carrier protein or a HA fusion protein is used as the antigen. Keyhole limpet haemocyanin (KLH) or bovine serum albumin (BSA) were preferably used as carrier proteins. Subsequently B lymphocytes were isolated from the spleen of the animals and immortalized by cell fusion with suitable myeloma cells or by other known methods such as e.g. by means of oncogenes (Jonak, Z.L. et.al., (1988) Adv. Drug Rev. 2:207-228) or in an electrical field (Zimmermann, U. (1982), Biochim. Biophys. Acta 694:227-277). The cell fusion was preferably carried out according to the invention with spleen cells of Lou/C rats and myeloma cells from the mouse line P3x63-Ag8,653 (Kearney, J.F. et al (1979), J. Immunol. 123, 1548-1550).

In this process the lymphocytes and the myeloma cells are fused by known methods, in particular by polyethylene glycol fusion (PEG), virus fusion or electrofusion and the hybrid cells (cell clones) that are formed are also selected by known methods such as e.g. by using selection media.

Thus for example positive clones were firstly tested with HA peptides and then with HA fusion proteins. In a first screen a biotinylated HA peptide e.g. Bio-C-HA (acetyl-**YPYDVPDYA**GSGSK (ε-biotinoyl)-amide) or Bio-N-HA (biotinoyl-ε-Aca-SGSG**YPYDVPDYA**-amide) was used and a HA-tagged glutathione-S-transferase (GST) was used in a second screen. Clones that were again positive were subsequently examined with regard to their affinity with the aid of plasmon resonance in a ~~BiaCore~~BIACORE® (registered trademark of Biacore AB) system and they were selected.

The hybrid cells were cloned, cultured and multiplied according to known methods and optionally stored in liquid nitrogen.

- the hybridoma supernatants selected in the 1st screen were again used undiluted and added to the coated MTP,
- the bound antibodies were detected with the aid of anti-rat-POD conjugate/TMB substrate.

3rd/4th Screen

- ~~BiaCore~~BIACORE® measurements were carried out with an analogous coating.

Result

5 clones with the highest affinity and the longest half-time of dissociation were selected with the aid of plasmon resonance in the ~~BiaCore~~BIACORE® system. They were named R 3F10, R 3A12, R 6D12, R 4H10 and M5B9. The affinity was only slightly different depending on the biotinoylated position of the peptides (C-~~terminus~~ terminus or N-terminus cf. Fig. 1).

The clones R 3F10, R 3A12 and R 6D12 were established as cell lines. They exhibit a good growth and a stable antibody production, and the antibodies that are produced have a 10-fold to 100-fold higher affinity than the monoclonal antibodies of the prior art 12CA5 and anti-HA BabCo.

Fig. 1 shows the affinities of the mABs according to the invention compared to the mAB 12CA5 and anti-HA BabCo.

Example 2

Determination of the affinity constants as well as of the rate constants of association and dissociation of the antibodies that are produced

The affinity constants and rate constants of association and dissociation of the antibodies that were produced was determined with ~~BIAcore~~®BIACORE® from the Pharmacia

18. [An antibody comprising a] A monoclonal antibody having an affinity of $> 10^8$ M^{-1} [against the epitope] for the amino acid sequence YPYDVPDYA, (SEQ ID NO: 1) as determined using a BIACORE® surface plasmon resonance system, wherein said monoclonal antibody is raised against a 13- or 14-amino acid containing epitope of human influenza virus haemagglutinin.

19. [An antibody comprising a] A monoclonal antibody having an affinity of 10^9 - 10^{10} M^{-1} [against the epitope] for the amino acid sequence YPYDVPDYA, (SEQ ID NO: 1) as determined using a BIACORE® surface plasmon resonance system, wherein said monoclonal antibody is raised against a 13- or 14-amino acid containing epitope of human influenza virus haemagglutinin.

20. The monoclonal antibody of claim 18 or claim 19, wherein said antibody is produced by hybridomas which are obtained by fusing mouse P3x63-Ag8.653 myeloma cells with B lymphocytes from Lou/C rats, said Lou/C rats having been immunized with a haemagglutinin peptide.

21. The monoclonal antibody of claim 18 or claim 19, wherein said antibody is produced by hybridomas which are obtained by fusing mouse P3x63-Ag8.653 myeloma cells with B lymphocytes from Lou/C rats, said Lou/C rats having been immunized with a haemagglutinin peptide, wherein said immunization is carried out with a haemagglutinin peptide coupled to keyhole limpet haemocyanin.

22. The monoclonal antibody of claim 18 or claim 19, wherein said antibody is produced by hybridoma R 3A12 deposited at the "Deutsche Sammlung für Mikroorganismen und Zellkulturen" under [the] Accession No. DSM ACC2286 (08.10.1996).

23. A method for the production of a monoclonal antibody against the epitope YPYDVPDYA (SEQ ID NO: 1) comprising:
(a) synthesizing a haemagglutinin peptide,
(b) immunizing a small mammal with said peptide,
(c) isolating B lymphocytes from the spleen of said mammal and fusing said lymphocytes with mouse P3x63-Ag8.653 myeloma cells to form clones,
(d) selecting clones formed in step (c) that produce an antibody which binds to a haemagglutinin peptide and to a haemagglutinin fusion protein, and
(e) selecting a clone [with a high affinity] from those selected in step (d) that produces an antibody with an affinity of $> 10^8\ M^{-1}$ for the sequence YPYDVPDYA and establishing said clone as a hybrid cell line.

24. The method of claim 23, wherein said haemagglutinin peptide is selected from the group consisting of acetyl-YPYDVPDYAGSGSK (ε-biotinoyl) amide (a derivative of SEQ ID NO: 2) and biotinoyl-ε-Aca-SGSGYPYDVPDYA amide (a derivative of SEQ ID NO: 3).

25. The method of claim 23, wherein said haemagglutinin fusion protein is haemagglutinin-tagged glutathione-S-transferase.